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DEPARTMENT OF MICROBIOLOGY

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April 18, 1973

Dr. Joshua Lederberg.  
Department of Genetics  
Stanford University Medical Center  
Stanford, California 94305

Dear Josh,

I am responding to your questions concerning my affair with B. subtilis transformation. I had not worked with B. subtilis prior to 1957. At about this period I was involved in studies of E. coli B spheroplast infection by shocked T2 phage (P.N.A.S. 43: 694-701, 1957). I was then led into a futile attempt to transform E. coli B spheroplasts. I spent considerable time and effort to put E. coli cultures into a state of competence (partial protoplasts, etc.) and at times thought it could be done. After considerable frustration, I decided to try to transform with germinating spores ("partial protoplasts") a number of strains of B. subtilis which Charlie Yanofsky had in the laboratory. One of these strains, 168, was transformed on the first try. The idea of using germinating spores arose from a discussion with Charlie, but, the notion of partial protoplasts in the germination process turned out to be incorrect. Even so, the idea of a unicleate cell system was intriguing. Nevertheless, the use of spores for synchronous growth leading to a competence stage was useful, even though impractical.

I was not at the time aware of Manninger's work. I was simply fortunate that Charlie Yanofsky stimulated me to try this organism. By hindsight, I was naive about competence of spheroplasts and although I recognized that DNases were deleterious in the E. coli system, did not definitively approach this problem. It is amazing that the competence problem has not yet been adequately defined, although I believe the issues are becoming clearer.

I was of course well aware of Avery's work. I had heard about the work from my teachers at Cal Tech (although I did not agree with some of the interpretations), and therefore read the paper with great excitement. I believed it, yet had some reservations about the effect of deoxyribonuclease. You may recall that in my paper on spheroplast infection, I found the effect of a crystalline DNase preparation (protease contamination) to be spurious, but Fraser and Mahler in their first paper (in the same issue of P.N.A.S.) fell into the trap.

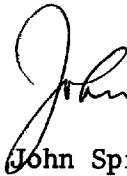
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Incidentally, the essential requirement for a protein component of tranfecting Ø29 DNA was demonstrated by Hirokawa (P.N.A.S. 69:1555-9, 1972).

Perhaps it is true that Avery's paper did not have as much impact as your (and Tatum's) work on recombination. This is probably due to the emphasis on the chemistry of the transforming principle rather than on the genetic aspects. I am convinced you were more persuasive.

Best regards.

Sincerely,

A handwritten signature in cursive script, appearing to read 'John', with a long horizontal stroke extending to the right.

John Spizizen, Ph.D.

JS:ck